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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/788,074	02/16/2001	Gokhan S. Hotamisligil	21509-044	4331

30623 7590 06/16/2004

MINTZ, LEVIN, COHN, FERRIS, GLOVSKY  
AND POPEO, P.C.  
ONE FINANCIAL CENTER  
BOSTON, MA 02111

EXAMINER
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ZARA, JANE J

ART UNIT	PAPER NUMBER
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1635

DATE MAILED: 06/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/788,074

Applicant(s)

HOTAMISLIGIL, GOKHAN S.

Examiner

Jane Zara

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 24 March 2003.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 16,22-24,27 and 31-36 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 16,22-24,27,31-36 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

### **DETAILED ACTION**

This Office action is in response to the communication filed 3-24-03.

Claims 16, 22-24, 27 and 31-36 are pending in the instant application.

### ***Response to Arguments and Amendments***

#### **Withdrawn Rejections**

Any rejections not repeated in this Office action are hereby withdrawn.

#### **Maintained Rejections**

Claims 16, 22-24, 27, 31-36 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention, for the reasons of record set forth in the Office action mailed 9-24-03.

Applicant's arguments filed 3-24-04 have been fully considered but they are not fully persuasive. Applicants argue that the results demonstrating both loss of function and gain of function are consistent and confirm the scientific basis and reliability of the claimed methods. Applicants' arguments are persuasive in part. A role of the fatty acid binding protein, Mal1, in obesity and insulin resistance has been shown in several ways in the instant disclosure. A correlation of a reduction in Mal1 expression in knockout mice (in ob/ob-mal1<sup>-/-</sup> mice) with a decrease in insulin resistance, or an improvement in insulin sensitivity, was demonstrated. In addition, a correlation between increased Mal1 expression and increased insulin resistance, or a reduction in insulin sensitivity,

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was also demonstrated in the instant disclosure (in transgenic mice overexpressing Mal1 from the fatty acid binding protein-4, aP2, promoter/enhancer). These results obtained in appropriate animal models for human obesity suggest Mal1 to be a marker for screening for insulin resistance in mammalian (including human) populations. The correlation of reduced Mal1 expression and increased insulin resistance in the obesity model for diabetes, as determined by performance in insulin and glucose tolerance tests, provide a correlation between changes in Mal1 expression and insulin resistance in appropriate mouse models for human obesity and diabetes. Consistent with this model, the instant disclosure also teaches a correlation between changes in body weight, circulating lipids and systemic insulin sensitivity with changes in mouse Mal1 transcript expression.

The instant disclosure fails, however, to teach a correlation between the quantitation of expression of the human Mal1 transcript with changes in insulin sensitivity. The instant disclosure also fails to provide any quantitation of mouse or human Mal1 polypeptide, or any changes in Mal1 polypeptide expression with changes in insulin sensitivity. The correlation of changes in mouse Mal1 transcript expression in loss-of-function or gain-of-function Mal-1 mouse models with changes in insulin resistance is not enabling for the ability to measure incremental changes in the expression of Mal1 transcript or polypeptide in a human. No evidence has been provided in the instant disclosure for the ability to measure incremental changes (e.g. 5, 10 or 20%) in the expression of Mal1 transcripts in mice or humans, whereby a correlative change in insulin resistance

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is observed. No evidence has been provided in the instant application to measure any level of Mal1 polypeptide in human or mouse. Furthermore, no evidence has been provided in the instant disclosure to correlate changes of Mal1 polypeptide expression with changes in insulin resistance. Therefore the instant 112, first paragraph rejection is maintained for lacking enablement over the scope claimed.

***Allowable Subject Matter***

SEQ ID No: 4 appears to be free of the prior art of record.

***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

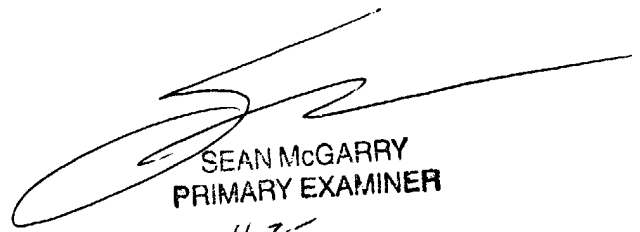
A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the mailing date of this final action.

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Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. **NO DUPLICATE COPIES SHOULD BE SUBMITTED** so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765**. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

JZ  
6-7-04

  
SEAN MCGARRY  
PRIMARY EXAMINER  
1635